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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/678,786	10/03/2003	Rachel Meyers	MPI00-317P1RCN1M	8269

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MILLENNIUM PHARMACEUTICALS, INC.
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EXAMINER	
KOSSON, ROSANNE	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 09/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	**Application No.** 10/678,786	**Applicant(s)** MEYERS ET AL.
	Examiner Rosanne Kosson	**Art Unit** 1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 01 September 2006.
2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.
3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 25-38 is/are pending in the application.
4a) Of the above claim(s) 25-30 and 35 is/are withdrawn from consideration.
5)☐ Claim(s) _____ is/are allowed.
6)☒ Claim(s) 31-34 and 36-38 is/are rejected.
7)☐ Claim(s) _____ is/are objected to.
8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.
10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a)☐ All b)☐ Some * c)☐ None of:
1.☐ Certified copies of the priority documents have been received.
2.☐ Certified copies of the priority documents have been received in Application No. _____.
3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicants' election without traverse of Group I, claims 31-38, in the reply filed on September 1, 2006 is acknowledged. Claims 25-30 and 35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim. No claims have been amended, canceled or added. Accordingly, claims 31-34 and 36-38, to the extent that the claims read on the invention that the polypeptide in the screening assay is an isolated polypeptide or a membrane-bound form of the isolated polypeptide only are examined on the merits herewith.

Claim Rejections - 35 USC § 101 and § 112, first paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

As in the parent application, the pending claims have been reviewed in light of the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. 112, first paragraph, Written Description Requirement, Federal Register, Vol. 66, No. 4, pages 1092-1111, January 5, 2001.

The following definitions in evaluating the claims for utility are pertinent.

"Specific" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention.

"Substantial" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

"Credible" - Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of Applicants' assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

"Well-established" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

Claims 31-34 and 36-38 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility. This rejection was discussed in parent Application No. 09/916,790. As discussed in the parent case, which claims a screening method for identifying any compound that binds to SEQ ID NO: 2, the protein with the predicted amino acid sequence of SEQ ID NO: 2 is expected to be a kinase based on sequence homologies with other protein kinases, and should have at least one Ser/Thr kinase site (not identified for SEQ ID NO: 2). The protein exhibits unidentified "32374 activity", modulates unidentified 32374-mediated activities and is involved in unidentified 32374-mediated or related disorders. The protein has several putative structural features, including a kinase domain. The protein was not expressed from its cDNA. The protein has no experimentally confirmed kinase or other activity and no known substrate. The protein has not been linked to any specific disease, and the protein has not been linked to the generation or the sensation of pain of any type. The instant application claims a screening method for identifying a compound that can treat a pain disorder, comprising performing steps to determine whether or not a particular compound binds to the protein of SEQ ID NO: 2, and then administering a compound that does bind to SEQ ID NO: 2 to an animal to determine whether or not that compound modulates (decreases) pain. But, the specification does not disclose what specific sort of pain is associated with the protein of SEQ ID NO: 2. Pain in humans arises in vastly different scenarios, from stubbing one's toe, to sore throat pain, to pain from major surgery, to diseases such as cancer.

The claimed protein, SEQ ID NO: 2, is not supported by a specific utility because the disclosed uses of the protein are not specific and are generally applicable to a wide variety of proteins. The polypeptide may be used, for example, to generate antibodies (page 45, lines 30, 31; page 42, line 1; page 50, lines 24-30; page 51, 52) or fusion proteins (page 47, lines 28-31; page 48), or to treat disorders characterized by insufficient or excessive production of 32374 protein or its substrate or inhibitors (page 58, lines 26-31), or to evaluate compounds for their ability to bind to the 32374 polypeptides (page 59, lines 7-15), or in screening assays for candidate compounds (page 59, lines 18-31; page 60-67). The molecules can be used as surrogate markers for unspecified disorders (page 82, lines 5-31; page 83; page 84, lines 1-6). These are non-specific uses that are applicable to proteins in general and not particular or specific to the protein being claimed. Any protein may be used in a screening assay to see what binds to it (see pp. 59-61 of the specification).

The protein of SEQ ID NO: 2 does not have a substantial utility, because the assertions about its structure and functions are not sufficient to determine that this protein is indeed a protein kinase and are not sufficient to establish that a substrate exists upon which the protein acts or that a signaling pathway exists in which SEQ ID NO: 2 is involved. Therefore, Applicants' assertions about the structure and function of the protein require further investigation in order to confirm them. Also, the specification does not disclose any connection between SEQ ID NO: 2 and any disease or condition that produces any sort of pain or between SEQ ID NO: 2 and pain.

As previously discussed, Applicants have referred to several known sequences which have sequence similarity to SEQ ID NO: 2. Applicants assert that a kinase domain is present in SEQ ID NO: 2 and that SEQ ID NO: 2 is similar to known Ser/Thr_kinases, but it is not clear from the facts presented by Applicants that the sequences with which comparisons were made are proteins with known Ser/Thr kinase function. Sequence comparisons of the putative kinase domain of SEQ ID NO: 2 with kinase domains from the ProDom database suffer from the following deficiencies:

1) comparison with ProDom consensus sequence of SEQ ID NO: 8 (not known to be a functional kinase domain) was performed for amino acids 226-285 of SEQ ID NO: 2 (60 amino acid fragment), even though on page 14 Applicants assert that the kinase domain of the polypeptide with SEQ ID NO: 2 extends from amino acid 1 to about 231;

2) comparison with ProDom consensus sequence of SEQ ID NO: 9 (not known to be a functional kinase domain) was performed for amino acids 321-346 of SEQ ID NO: 2 (26 amino acid fragment), even though on page 14 Applicants assert that the kinase domain of the polypeptide with SEQ ID NO: 2 extends from amino acid 1 to about 231;

3) comparison with ProDom consensus sequence of SEQ ID NO: 10 (not known to be a functional kinase domain) was performed for amino acids 166-245 of SEQ ID NO: 2 (80 amino acid fragment), and there was only 30% identity over the 80 amino acids in this region;

4) comparison with ProDom consensus sequence of SEQ ID NO: 15 (not known to be a functional kinase domain) was performed for amino acids 30-189 of SEQ ID NO: 2 (160 amino acid fragment), and there was only 22% identity over the 160 amino acids in this region;

5) comparison with ProDom consensus sequence of SEQ ID NO: 16 (not known to be a functional kinase domain) was performed for amino acids 29-262 of SEQ ID NO: 2 (234 amino acid fragment), and there was only 26% identity over the 234 amino acids in this region, amino acids 232-262 being outside the previously defined kinase domain.

Therefore, the sequence comparisons presented by Applicants do not convincingly show a functional kinase domain in the protein of SEQ ID NO: 2. Additionally, Applicants have not provided any evidence that the kinase of SEQ ID NO: 2 has a substrate.

A search of SEQ ID NO: 2 in the protein sequence databases indicates that it is 100% identical to the human sequence of Wei et al. (US 2002/0103116 A1) (Wei et al.'s SEQ ID NO: 2) and 93.7% identical to SEQ ID NO: 2 of Mitsubishi Chemical Corp. (JP 2000-060571 A) (see enclosed alignments). Neither of these two proteins has been shown to be a protein kinase, and their amino acid sequences and functions are putative.

To summarize, sequence comparisons presented by Applicants and the conclusion based on these comparisons regarding the function of with SEQ ID NO: 2 were not found convincing. Therefore, the protein of SEQ ID NO: 2 does not have a specific utility or a substantial utility. To demonstrate the required utility, the protein would have to be expressed and shown to be a kinase. Its regulators or substrates would have to be identified, and an association with a disease state in which an animal subject suffers pain would have to be demonstrated, the kinase activity of SEQ ID NO: 2 either contributing to or inhibiting pain. Most importantly, Applicants would have to demonstrate that inhibiting or enhancing the kinase activity of SEQ ID NO: 2 relieves pain in the affected subject. In the absence of any disclosed relationship between Applicants' SEQ ID NO: 2 and pain associated with any disease or condition, the claimed method lacks a specific and a substantial utility. Any information obtained from data mining such as sequence comparisons would only serve as the basis for further research on the observation itself. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner*, 148 USPQ at 696. The disclosure therefore does not present a substantial utility that would support the requirement of 35 U.S.C. §101.

Applicants should explicitly identify a specific and substantial utility for the claimed invention and establish a clear relationship between any evidence of record and the claimed invention.

Claims 31-34 and 36-38 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112, first paragraph

Claims 31-34 and 36-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, as discussed above, the specification does not disclose that the protein of SEQ ID NO: 2 is associated with any disease or condition in which a subject experiences pain. The specification does not disclose that the putative kinase activity of SEQ ID NO: 2 either causes or inhibits pain. Additionally, the specification does not provide any evidence that a compound that binds to SEQ ID NO: 2 can modulate- presumably decrease- pain.

Also, with respect to claim 37, this claim recites that the binding of the test compound to SEQ ID NO: 2 may be detected in an assay for any activity of SEQ ID NO: 2. The only activity discussed in the specification for SEQ ID NO: 2 is protein kinase activity, although this activity has not been demonstrated.

The factors to be considered in determining whether or not undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir.1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the relative skill of those in the art, (5) the predictability or unpredictability of the art, (6) the amount or direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary. Although the quantity of experimentation alone is not dispositive in a determination of whether the required experimentation is undue, this factor does play a central role. For example, a very limited quantity of experimentation may be undue in a fledgling art that is unpredictable where no guidance or working examples are provided in the specification and prior art, whereas the same amount of experimentation may not be undue when viewed in light of some guidance or a working example or the experimentation required is in a predictable established art. Conversely, a large quantity of experimentation would require a correspondingly greater quantum of guidance, predictability and skill in the art to overcome classification as undue experimentation. In Wands, the determination that undue experimentation was not required to make the claimed invention was based primarily on the nature of the art, and the probability that the required experimentation would result in successfully obtaining the claimed invention. (Wands, 8 USPQ2d 1406). Thus, a combination of factors which, when viewed together, would provide an artisan of ordinary skill in the art with an expectation of successfully obtaining the claimed invention with additional experimentation would preclude the classification of that experimentation as undue. A combination of Wands factors, which provide a very low likelihood of successfully obtaining the claimed invention with additional experimentation, however, would render the additional experimentation undue.

1.Breadth of the claims.

The claims are very broad because they recite a screening assay in which any compound that binds to the protein of SEQ ID NO: 2 may be administered to an animal and tested for its ability to modulate (decrease) pain.

2. The nature of the invention.

The invention is designed to provide a novel screening assay for analgesic compounds.

3. The state of prior art.

The prior art does not provide hard evidence that SEQ ID NO: 2 is a kinase, that it is linked to any disease or condition that is associated with pain, that the activity of SEQ ID NO: 2 (kinase or otherwise) causes or inhibits pain, or that any compound that binds to SEQ ID NO: 2 can increase or decrease pain in a subject.

4. The relative skill in the art.

The relative skill in the art as it relates to the method of the invention is characterized by that of a M.D. or Ph. D. level individual.

5. The level of predictability in the art.

Because it is not known definitively that SEQ ID NO: 2 is a kinase, that it is linked to any disease or condition that is associated with pain, that the activity of SEQ ID NO: 2 (kinase or otherwise) causes or inhibits pain, or that any compound that binds to SEQ ID NO: 2 can increase or decrease pain in a subject, the specification needs to have more detail as to how to make and use the invention. Because the prior art and the instant specification do not disclose the necessary information, it cannot be predicted that one of skill in the art can screen for compounds that increase or decrease pain by screening for compounds that bind to SEQ ID NO: 2 (enhancers of kinase activity if SEQ ID NO: inhibits pain and inhibitors of kinase activity if SEQ ID NO: 2 causes pain).

6. The amount of guidance present.

Applicants have not provided any specific guidance for a screening assay in which compounds are tested for their ability to bind to SEQ ID NO: 2. Thus, it is not known that any compound binds to SEQ ID NO: 2, either specifically or non-specifically. Applicants have also not provided any specific guidance for administering such ligands to animals in a pain model assay and for determining the effect of such ligands on pain.

7. The existence of working examples.

The specification does not contain any working examples in which compounds are tested for their ability to bind to SEQ ID NO: 2. Thus, the specification does not contain any working examples in which compounds that bound to SEQ ID NO: 2 were administered to animals and tested for their ability to increase or decrease pain.

8. The quantity of experimentation necessary.

To prove that one of skill in the art could identify a compound that treats pain by screening for compounds that bind to the protein of SEQ ID NO: 2, a number of additional experiments would have to be conducted. In these experiments, a kinase assay for SEQ ID NO: 2 would first have to be developed. Thus, substrates that could be phosphorylated by SEQ ID NO: 2 would have to be found, and detection agents that distinguish the phosphorylated and unphosphorylated forms would have to be prepared and tested. Secondly, the kinase activity of SEQ ID NO: 2 would have to be demonstrated. Thirdly, an association between the kinase activity of SEQ ID NO: 2 and pain in a subject would have to be demonstrated. Fourthly, the relationship between blocking the kinase activity of SEQ ID NO: 2 and a decrease in pain or the relationship between enhancing the kinase activity of SEQ ID NO: 2 and a decrease in pain would have to be demonstrated. A number of different compounds that are ligands of SEQ ID NO: 2 would have to be identified and tested for their pain-altering properties on a subjects, and a large number of subjects that are various types of animals would have to tested. For each type of animal, a range of doses of the analgesic or pain-altering compound would have to be tested.

These types of experiments and data are missing from the specification. A great deal of guidance is needed to establish that compounds that modulate pain can be identified by screening for compounds that bind to SEQ ID NO: 2, because this screening assay is claimed, and no evidence that SEQ ID NO: 2 is associated with disease or pain is provided. Even if one such compound could be identified, after developing all of the required reagents and assays as described above, without establishing all of the required disease associations as described above, such a screening assay could not be predicted to identify a second compound that modulates pain.

Regarding claim 37 (assaying for activities other than kinase activity), the relevant Wands factors listed above are (3) and (5) – (8). The prior art does not disclose that SEQ ID NO: 2 has kinase activity, nor does it disclose that SEQ ID NO: 2 has additional activities that may be assayed (3). The specification provides no guidance or working examples for SEQ ID NO: 2 having kinase or other activities (6 and 7). Based on the specification, it cannot be predicted that SEQ ID NO: 2 has kinase or other activities (5). Because supporting evidence is lacking in the prior art and in the specification, undue experimentation would be required to determine that SEQ ID NO: 2 has kinase and other activities.

Therefore, the claims fail to satisfy the enablement requirement.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rosanne Kosson whose telephone number is 571-272-2923. The examiner can normally be reached on Monday-Friday, 8:30-6:00, alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber, can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rosanne Kosson
Examiner, Art Unit 1653

rk/2006-09-19

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